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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,401	01/16/2002	Alfred Pollak	7126-2	8318

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KRAMER LEVIN NAFTALIS & FRANKEL LLP
INTELLECTUAL PROPERTY DEPARTMENT
1177 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 10/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,401	POLLAK ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/5/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-31,33-42 and 45-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-31,33-42 and 45-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

WITHDRAWAL OF FINALITY

1. The finality of the rejection of the last Office action is WITHDRAWN because having reviewed the instant application, the following action is deemed necessary in order to clarify the instant invention and record.

ACKNOWLEDGMENTS

2. The Examiner acknowledges receipt of the amendment filed 10/5/06 wherein claims 1, 7, 9, 10, 17, 35, 38, 39, 41, and 42 are amended and claims 15, 32, 43, and 44 are canceled.

Note: Claims 1-14, 16-31, 33-42, and 45-49 are pending.

RESPONSE TO APPLICANT'S ARGUMENTS/AMENDMENT

3. The Applicant's arguments and/or amendment filed 10/5/06 to the rejection of the claims made by the Examiner under 35 USC 103 have been fully considered and deemed persuasive. Therefore, in view of the amendment and arguments presented 10/5/06, all outstanding rejections are hereby WITHDRAWN.

NEW GROUNDS OF REJECTIONS

112 First Paragraph Rejections

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 26-30, 33, 34, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The claims are directed to methods of detecting the presence, therapy, or assessing the severity of an oncological, neurological, inflammatory, infectious, or degenerative disease, disorder, or abnormal physical state by administering a composition comprising a metal support surface, ligand, targeting moiety, and metal ion.

(2) State of the prior art

The state of the prior art indicates that cancer therapy, for example, remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol as well as detection of the cancers. It is known (see Golub et al., Science, October15, 1999, pp. 531-537) that the challenge of cancer treatment, for example, has been to target specific therapies to pathogenetically distinct tumor types in order to maximize efficacy and minimize toxicity. The classification of cancer has been based primarily on morphological appearance of the tumor and that of tumors with similar histopathological appearance may follow significantly different clinical courses and have different responses to therapy (see Golub et al., Science, October15, 1999, pp. 531-537). As a result, there is no absolute predictability of which tumors are treatable, even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the knowledge in the art would hinder one of ordinary skill in the art from accepting any therapeutic regimen as being acceptable for all tumor/cancer treatments. Additionally, for example, infection is a process that can take place in virtually any part of the body. Thus, there is a vast range of infectious diseases that may occur based on the various biochemical pathways. Also, oncology which deals with the study of neoplasms (tumors) may occur in many areas of the body. Neurology which deals with the branch of medicine involving the nervous system and its diseases may result in a wide range of diseases and disorders of the body. Inflammation which is a tissue's reaction to irritation, infection, or injury may occur in virtually any part of the body.

Hence there is not predictability in identifying the diseases and disorders encompassed by the instant invention.

(3) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high. There is no evidence of record which would enable the skilled artisan in the identification of the patients who have the potential of becoming afflicted with the numerous diseases or disorders that are encompassed by the instant invention. The assumption that the metal support surface, ligand, targeting moiety, and metal ion may be used to treat/detect all diseases and disorders embraced by the claims is an incredible finding for which Applicants have not provided supporting evidence. Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the compositions and methods used in treating/detecting any or all diseases as claimed.

(4) Level of predictability in the art

The art pertaining to the treatment/detection of diseases is highly unpredictable. Determining the various types or classes of diseases/disorders treatable/detectable with the instant invention requires various experimental procedures and without guidance that is applicable to all diseases and disorders, there would be little predictability in performing the claimed invention.

(5) Amount of direction and guidance provided

There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the numerous diseases/disorders or the various methods by which detection of the

diseases/disorders occur as claimed herein. Applicant's limited guidance does not enable the public to prepare such a numerous amount of compositions and methods for treating and detecting the unlimited number of diseases and disorders encompassed by the claims. There is no directional guidance for the types or classes of diseases/disorders that are treatable or detectable by the instant invention. The evidence of record does not provide information as to exactly what diseases/disorders Applicant is treating or detecting. Hence, there is no enablement for all possible diseases/disorders treatable with the claimed composition.

(6) Existence of working examples

The claims encompass a vast number of diseases and disorders. Applicant's limited working examples do not enable the public to prepare such a numerous amount compositions and treat and detect a vast number of diseases/disorders.

(7) Breadth of claims

The claims are extremely broad due to the vast number of possible diseases/disorders known to exist. . For example, there are may classes of diseases such as allogeneic, communicable, congenital, contagious, deficiency, endemic, functional, hereditary, infectious, local, occupational, organic, periodic, social, systemic, and venereal diseases that are known to affect a subject. In addition, it is notes that the claims read on oncological, neurological, inflammatory, infectious, and degenerative diseases, disorders, and abnormal physical states.

(8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification fails to enable the skilled artisan to practice the invention without undue experimentation. Furthermore, based on the unpredictable nature of the invention, the state of the prior art, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

112 Second Paragraph Rejections

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-14, 16-31, 33-42, and 45-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-14, 16-31, 33-42, and 45-49: The claims as written are ambiguous because one cannot readily ascertain what is being claimed. For example, in independent claim 1, it appears if the metal has been omitted form the metal ion labeled agent. In other claims (e.g., claim 4, it appears as if Applicant is listing the targeting molecule, not the conjugate. In other claims (e.g., claim 24), it appears as if Applicant intended to have method, not product claims. In other claims (e.g., claim 26), it is unclear what disease(s)/disorder(s) are being assessed/detected and the manner in which the detection/assessing is conducted. In other claims (e.g., claim 38), it appears as if the claim depend upon the wrong claim (e.g., claim 38 should depend form claim

37, not 27). In other claims (e.g., claim 38), it is unclear if Applicant is referring to the cysteine amino acid residue or not. In addition, in some of the claims (e.g., claim 45), it is unclear what accessory groups are applicable to the instant invention. Thus, claims depending upon the independent and intervening claims are also vague and indefinite since one cannot ascertain what is being claimed. *Hence, the following suggestions are made in order to clarify the instant invention and correct some of the inconsistencies and problems with the claims as now written.*

Claim 1, line 10, add ' and (c) a complex-forming metal ion'.

Claim 4, line 1, replace 'conjugate' with 'targeting molecule'.

Claim 5, line 1, replace 'conjugate' with 'targeting molecule'.

Claim 6: Delete claim.

Claim 7: The limitations of claim 10 should be incorporated into claim 10.

Claim 8, line 1, replace 'ligand' with 'targeting molecule'.

Claim 9: Delete 'N_xS_{4-x}'.

Claim 10: Delete claim.

Claim 14, line 1, delete 'claim 6 or'.

Claim 16, line 2, replace 'comprises' with 'is'.

Claim 19, rewrite claim: A method of generating a complex-forming metal ion labeled diagnostic agent or radiotherapeutic agent comprising contracting the composition of claim 1 with a metal ion to form a coordinate bond between the metal ion and conjugate so that the labeled conjugate is released from the support.

Claim 20, rewrite claim: The method of claim 19 further comprising collecting the labeled conjugate released.

Claim 21: Delete claim.

Claim 22, rewrite claim: A method of preparing a technetium or rhenium labeled agent comprising contacting the composition of claim 1 with 99mTc that has a specific activity greater than 10,000 Ci/mmol or with 188Re that has a specific activity of greater than 3,000 Ci/mmol.

Claim 23: The method of claim 22 further comprising a peptide comprising dimethylglycylserinylcysteinylglycine.

Claim 24: A pharmaceutical composition comprising a composition according to claim 1 and a pharmaceutically acceptable carrier.

Claim 26: A method of imaging a mammal comprising

(a) administering an effective amount of the composition of claim 24; and

(b) generating an image of the mammal.

Claim 27: A method of radiotherapy in a mammal comprising administering an effective amount of the composition of claim 1 to a subject.

Claim 28: The method of claim 26 wherein the composition is administered intravenously.

Claim 29: The method of claim 26 wherein the composition administered to the mammal is about 0/01 mcg/kg/minute to 1,000 mcg/kg/minute.

Claim 30: The method of claim 29 wherein the composition administered to the mammal is about 0.01 to 50 mcg/kg/minute.

Claim 33: The method of claim 26 wherein the mammal is imaged by a technique selected from the group consisting of positron emission tomography, nuclear magnetic resonance imaging, scintigraphy, single photon emission computed tomography, perfusion contrast echocardiography, ultrafast x-ray computed tomography, and digital subtraction angiography.

Claim 34: The method of claim 33 wherein the technique is single photon emission computed tomography.

Claim 35: after 'agarose' in the last line of the claim insert 'the conjugate comprises a ligand and a targeting molecule'.

Claim 35, lines 1-2, delete 'for preparing a complex-forming metal ion labeled agent, the kit'.

Claim 36: The kit of claim 35 wherein the ligand comprises a sulfur atom attached to a sulfur protecting group.

Claim 37: The kit of claim 35 wherein the ligand comprises a sulfur or phosphorous for binding to the metal support surface.

Claim 38: The kit of claim 37 wherein the ligand comprises

(a) a surface binding group selected from the group consisting of a cysteine amino acids residue, a thiol or thioester group attached to an organic molecule having a molecular weight less than about 600 Daltons, and a phosphorous containing organic molecule wherein the

cysteine amino acid residue or organic molecule releasably binds to the support surface; and

(b) at least one accessory group that coordinates with the metal wherein the accessory group is selected from the group consisting of:

a nitrogen atom, an oxygen atom, or a sulfur atom incorporated in an amino acid residue;

a nitrogen atom, an oxygen atom, a selenium atom, a phosphorous atom, or a sulfur atom incorporated into an amino acid residue;

a nitrogen atom, an oxygen atom, a selenium atom, a phosphorus atom, or a sulfur atom incorporated in an organic molecule; or

a combination of one or more of the accessory groups.

Claim 45: The composition of claim 1 wherein the ligand comprises and organic molecule having a molecular weight less than about 600 Daltons, said ligand further comprises:

(a) a sulfur atom in the form of a thiol or thioether group or a phosphorus atom where the sulfur or phosphorus atom binds to the support surface; and

(b) at least one accessory group that coordinates with the metal wherein the accessory group is selected from the group consisting of:

a nitrogen atom, an oxygen atom, or a sulfur atom incorporated in an amino acid residue;

a nitrogen atom, an oxygen atom, a selenium atom, a phosphorous atom, or a sulfur atom incorporated into an amino acid residue;

a nitrogen atom, an oxygen atom, a selenium atom, a phosphorus atom, or a sulfur atom incorporated in an organic molecule; or

a combination of one or more of the accessory groups.

Claim 46: The kit of claim 37 wherein the ligand comprises a organic molecule having a molecular weight of less than about 600 Daltons, said ligand further comprises:

(a) a sulfur atom in the form of a thiol or thioether group or a phosphorus atom where the sulfur or phosphorus atom binds to the support surface; and

(b) at least one accessory group that coordinates with the metal wherein the accessory group is selected from the group consisting of:

a nitrogen atom, an oxygen atom, or a sulfur atom incorporated in an amino acid residue;

a nitrogen atom, an oxygen atom, a selenium atom, a phosphorous atom, or a sulfur atom incorporated into an amino acid residue;

a nitrogen atom, an oxygen atom, a selenium atom, a phosphorus atom, or a sulfur atom incorporated in an organic molecule; or

a combination of one or more of the accessory groups.

Claims 47-49: Delete claims (Applicant is already claiming this subject in claims 26, 27, and 33).

Note: Applicant is respectfully requested to review the claim dependency of each of the pending claims.

COMMENTS/NOTES

8. The claims are distinguished over the prior art of record because the prior art neither anticipates nor renders obvious compositions, methods of making the compositions, and uses of the compositions comprising a metal support, ligand, targeting agent, and metal ion as set forth in independent claim 1.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

D. L. Jones
Primary Examiner
Art Unit 1618

October 16, 2006